

Application No.: 09/977,864

Docket No.: CIBT-P01-104

**REMARKS**

Claims 1, 5, 21, and 23-67 are pending and under consideration, prior to Amendment.

Claims 60, 61, 63, and 64 have been amended to clarify that the tumor or colon cancer tissue overexpresses a *gli-1* or *Sonic hedgehog* gene. Support for Applicants' amendments can be found, for example, throughout the specification and pending claims. No new matter has been entered.

Applicants have added new dependent claims 68-70. Support for the subject matter of the newly added claims is found throughout the specification and previously pending claims. No new matter has been entered.

Applicants request entry of Applicants' after-final amendment. Applicants' amendment either places the application in condition for allowance or simplifies issues for Appeal. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order in which they appear in the Office Action.

**Information Disclosure Statement**

Applicants note that the Information Disclosure Statements filed on August 28, 2008 and November 26, 2008 have been considered.

**Withdrawn Rejections**

Applicants note that the previous rejections of Claims 60 and 63-67 under 35 U.S.C. § 112, first paragraph and under 35 U.S.C. § 112, second paragraph have been withdrawn. Applicants also note with appreciation the withdrawal of the rejections of claims 61-67 under 35 U.S.C. § 112, first paragraph and the withdrawal of the provisional rejection of claims 64-66 under the judicially created doctrine of obviousness-type double patenting.

**Double Patenting**

Claims 1, 5, 21, 25, 26, 28, 30, 31, 35, 36, 38, 40-43, 50-53, 56, and 57 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claim 68 of co-pending Application No. 10/652,298.

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Claims 61 and 64-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claim 70 of pending Application No. 10/652,298.

Applicants ask that these rejections be held in abeyance until indication of allowable subject matter. Applicants will submit a terminal disclaimer, if necessary, upon indication of allowable subject matter.

Applicants note that, in accordance with MPEP 804.I.B, the Examiner will maintain the provisional double patenting rejection until there are either no longer any conflicting claims or the double patenting rejection is the only remaining rejection in at least one of the applications.

#### **Claim Objections**

Claim 64 was objected to due to a typographical error in which a term was not italicized consistently throughout the claim. Applicants have amended claim 64 to correct this typographical error. Applicants' amendment is made solely for consistency and does not alter the scope of the claim.

#### **35 U.S.C. § 112, 1st paragraph, enablement**

Claims 60-67 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. In particular, the term "expression" is alleged to encompass "overexpresses," "underexpresses," or no change in expression. The Examiner further asserts that the examples only disclose the effects of hedgehog antibodies on cells that overexpress *gli-1* or *Sonic hedgehog*.

Applicants respectfully traverse this rejection, and point out that the specification does not use the term "express" so generally. Applicants maintain that the term "expressing" is not used throughout the specification to generally refer to any of "overexpresses" "underexpresses" or no change, as the Examiner suggests. On page 39, paragraph [0542], expression is described in the context of activation: "expression of *gli-1* is activated by the hedgehog signaling pathway" indicating that *gli* gene expression is set into motion by hedgehog signaling. In turn, activation of *gli-1* gene expression activates expression of other genes: "the *gli* genes encode transcription factors

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that activate expression of many genes needed to elicit the full effects of hedgehog signaling." Finally, on page 53, paragraph [0687], the symbols "-", "+", and "++++" correspond to the expression of gli-1 mRNA in hyperproliferative cells of human tumors. Here, "-" refers to a level of expression that is no higher than that of non-proliferative cells on the same slides as the hyperproliferative cells, and clearly differs from "+", "++", "+++" and "++++" which all refer to increased levels of gli-1. Using this system, only samples showing "++" or higher levels of gli-1 expression are "considered to have substantially increased gli-1 expression."

While it is true that claims must be given their broadest *reasonable* interpretation, Applicants submit that the interpretation of "expression" proffered by the Examiner in the instant Office Action is not a reasonable interpretation of this term, as understood in the context of the instant specification.

Nevertheless and solely to expedite prosecution, Applicants have amended Claims 60, 61, 63, and 64 consistent with the Examiner's suggestion. Applicants' amendment is made solely to clarify that affected tissues contain, produce, replicate, or "express," more of these genes or gene products.

Applicants' amendment is not in acquiescence to the rejection. Applicants expressly reserve the right to prosecute claims using similar or differing language in this or future applications, as well as to present additional arguments to address the basis for this rejection. Applicants' amendment is believed to obviate the rejection, and reconsideration and withdrawal of this rejection are requested.

#### **Allowable Subject Matter**

Applicants note with appreciation that the Examiner has indicated that claims 32-34 and 44-49 are allowable. Further, the Examiner has indicated that claims 23, 24, 27, 29, 37, 39, 54, 55, 58, and 59 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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**Co-Pending Applications**

The Examiner is obviously aware of co-pending Application No. 10/652,298 (currently applied in the above noted double patenting rejection and also handled by Examiner Howard). Applicants invite the Examiner to consider all prior, ongoing, and future prosecution of co-pending Application 10/652,298 (the most recent action is a final Office Action, mailed on March 23, 2009).

With respect to the final Office Action mailed March 23, 2009 in co-pending Application 10/652,298, Applicants take this opportunity to draw the Examiner's attention to the rejection under 35 U.S.C. 112, first paragraph (enablement), and the references cited in support of that rejection. Applicants note that the substance of the enablement rejection made in the co-pending application is substantially the same as the substance of the enablement rejection advanced in the instant application. However, in addition to the references cited by the Examiner in alleged support of the enablement rejection made in the instant application, the Examiner cited the following three additional references in the co-pending application:

Schulz, 2006, *Int J Cancer* 119: 1513-1518.

Sheng et al., 2004, *Molecular Cancer* 3: 29 (doi: 10.1186/1476-4598-3-29)

Thayer et al., 2003, *Nature* 425: 851-856.

It appears to Applicants that these references were not cited by the Examiner in the instant application because the teachings of the references are not directed to species elected by Applicants' in the instant application. Further, Applicants note that the above references were used in the co-pending application to advance substantially the same argument as that supported by the references cited by the Examiner when making the enablement rejection in the instant application. Applicants respectfully submit that the amendments filed herewith address the instant enablement rejection, thereby obviating the relevance of the art of record and the above noted references. Nevertheless, Applicants take this opportunity to bring these additional references to the Examiner's attention.

Additionally, Applicants take this opportunity to update the Examiner on the status of various co-pending applications – the existence of which has already been brought to the Examiner's attention and made of record in this case. Applicants invite the Examiner to consider all prior, ongoing, and future prosecution in these co-pending applications. Application serial number

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09/804,490 issued November 4, 2008 as U.S. Patent No. 7445778. Application serial number 10/652,686 issued March 3, 2009 as U.S. Patent No. 7498304. The most recent action in application serial number 09/883,848 is a Final Office Action mailed March 3, 2008. The most recent action in application serial number 10/772,090 is a Non-final Office Action mailed October 9, 2008. The most recent action in application serial number 10/727,195 is an Non-Final Office Action mailed April 13, 2009.

### CONCLUSIONS

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for the same and request that the extension fee and any other fee required for timely consideration of this submission be charged to Deposit Account No. 18-1945 under order number CIBT-P01-104.

Dated: May 1, 2009

Respectfully submitted,

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